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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,830	01/05/2001	Katia Georgopoulos	10287-067001	5392

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,830	GEORGOPOULOS, KATIA	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 7-56* is/are pending in the application.

4a) Of the above claim(s) *11-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10 and 51-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a continuation-in-part of 08/283,300, filed July 29, 1994, now US Patent 6,172,278, which is a continuation-in-part of 08/238,212, filed May 2, 1994, now abandoned, and continuation-in-part of 08/121,438, filed September 14, 1993, now abandoned, and continuation-in-part of 07/946,233, filed September 14, 1992, now abandoned.

Applicants' amendment filed October 23, 2003, has been received and entered. Claims 2-6 were canceled. Claims 1 and 7 have been amended. Claims 51-56 have been added. Claims 1 and 7-56 are pending.

Election/Restriction

Claims 1 and 7-56 are pending. It is noted that newly added claims 51-56 are drawn to the elected invention. Claims 11-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 15. Claims 1, 7-10 and 51-56 are currently under examination.

Priority

As noted in the previous office action, Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: the

second application must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the second application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). In the instant case, the specific Ikaros transcriptional/promoter sequences instantly claimed are first presented in the instant application. Previous applications are silent with respect to teachings which would support the instantly product, and thus fail to fully support the elected invention under 35 U.S.C. 112, first paragraph.

Applciant has not addressed the issue of priority in the instant amendment, accordingly, as indicated previously the priority date given the pending claims is the filing date of the instant application.

Specification

The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. 37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description

or claims of the patent application. Upon review of the instant specification oligonucleotide sequences have been identified that do not have specific SEQ ID NOs (see for example: page 81, lines 22-25, page 84, lines 27-30). It is unclear whether these sequences are provided in the CRF/sequence listing or require a new sequence listing. It is recommended the Applicants review the entire disclosure for unidentified sequences and fulfil the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825.

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

In the instant, upon review of the portions of the specification indicated by Applicants to support the new amendments Examiner can not find literal or figurative support for the limitation of the specific size fragments associated with specific clusters set forth in claim, nor support for the use of SEQ ID NOs: 29 and 30 in providing an Ikaros promoter. Further, it is noted that SEQ ID NOs: 29 and 30 are listed in the sequence listing, however upon review of the entire specification Examiner can not identify these specific sequence identifiers. It is noted that the portions pointed to by Applicants provide general support for fragments of the Ikaros promoter, however they fail to provide specific support for the amendments as set forth in the claims.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1 and 51 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed,

involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 1, 7-10 stand rejected and newly added claims 51-56 are under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants reiterate the basis of the rejection and argue that the rejection has been overcome by the present amendments (page 9). Reviewing the amendments to the claims and limitations in newly added claims, Applicants argue the both explicit physical and chemical characteristics have been sufficiently set forth pointing to the written description guidelines for support of their arguments (bridging pages 9-10). Applicants argue that the sequences encompassed by the claims have been tested and are active and thus not merely putative promoters as demonstrated by their ability to drive expression of a G.P. reporter. See Applicants' amendment, pages 9-11. Applicants' arguments have been fully considered but not found persuasive.

Initially, it is noted that the claims set forth a physical limitation of a specific size and is implicitly a polynucleotide by the fact that it represents a restriction fragment (claim 1) or amplifiable sequence (claim 51), and by the fact that it is contained in a construct (dependent claims). However, none of the claims set forth any functional characteristic of the claimed sequences. Examiner acknowledges that the specification supports that the specific sequences set forth as SEQ ID NOs have been tested for promoter activity, however the instant claims encompass more than these specific SEQ ID NOs, embracing allelic variants, mutants if such exist, and require methods which are subject to variation depending on the artisan practicing the method or the source from which the starting material is derived. For example, as set forth in claim 1 EcoRI and BamHI are capable of providing at least three different size fragments. Moreover, a size of a fragment would be considered insufficient description of a specific sequence and would be dependent on the material from which it is derived. For example if genomic DNA from a human or mouse lymphoid cell was used, identification/isolation by size alone would not produce uniquely a Ikaros promoter fragment. More simply put, providing a sequence of a given size would not indicate it to be an Ikaros promoter. Only with further characterization of a given sequence of any given size could one determine if it represented a particular HSS Ikaros cluster, or if it even had any functional properties associated with an Ikaros promoter. With respect to the amplification with particular primers set forth in claim 51, initially it is noted that the specification does not specifically teach that the Ikaros promoter or what regions of the Ikaros promoter are generated with these primers. However, even if one were to

assume that the oligonucleotides could be used to amplify an Ikaros promoter, the issues involving the amplified product would be the same as set forth above. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

As set forth in the previous office action, the specification teaches that a genomic clone of the Ikaros gene has been isolated and the 5' end of said clone has been analyzed for DNAaseI hypersensitive sites (HHS). By analyzing cells of several different types by HHS, the disclosure teaches that the Ikaros gene may have two possible different promoters, and that the "putative promoters are associated with two distinct clusters of lymphoid-specific DNaseI HHS" (page 79, lines 25-30). The specification and the art of record is silent with respect to any specific sequence regarded as an Ikaros transcriptional control region or any teaching of what transcriptional factors are implicated in the control of the Ikaros transcriptional control region comprised on the large genomic clone. The only specific teaching for potentially important cluster regions of the genomic clone is the HHS analysis of various cell types. Again, the specification is silent with respect to any specific sequence for the Ikaros transcriptional control region, and it fails to provide any specific guidance to what transcriptional factors bind or regulate the Ikaros gene or the specific control region instantly claimed. Moreover, the specification is silent with respect to what would be defined as transcriptional control region. Besides the implication of particular regions of the genomic clone by HHS analysis in specific

cell types, there is no specific functional attributes described in the specification which would be considered indicative of an Ikaros regulatory element. Further, there is no specific definition of a control region being active or inactive in any particular context which clearly defines an assay to test whether a specific sequence is a or part of a Ikaros transcriptional regulatory region. It is noted that the specification sets forth the particular terms and embodiments recited in the claims, however the specification fails to provide any specific sequence or the necessary guidance to what the specific sequences comprised by the terms. The claims are broad encompassing an enormous number of species of Ikaros transcriptional control region from any species of organism. Further, the claims include fragments and specific clusters which have no specific defined activity. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, the specification provides literal support for the recited embodiments, however the specification fails to describe the relevant identifying characteristics of any of the nucleic acid sequences of any of the sequences encompassed by the claims. The portions of the specification discussed above are noted, however written description requires

more than a mere indication of "putative promoters" (page 79, line 27). Again, no specific sequence is taught in the specification nor the art of record. There is no evidence that these specific clusters observed by HHS analysis in one genomic clone are important to function or whether any alteration will result in a modification of activity, or if they are consistent with genomic sequences obtained from the same region of Ikaros of different species of animals. Absent any specific teaching of any sequence the skilled artisan can not envision all the possible variant nucleic acid sequences which are comprised by the instant claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated:

In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not

suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers,* 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.").

Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. In the instant case, Examiner would not contest that the Ikaros gene has a transcriptional control region, however in view of the teachings of the instant specification it is maintained that the artisan would not be able to distinguish any particular sequence as an Ikaros transcriptional control region. Further, even if a given sequence could be tested, no specific biological activity of the Ikaros control region or of any of the specific clusters has been clearly set forth to assay.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. In the instant case, the specification fails to describe even a single species of each enormous genus comprised by the claims, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met.

Therefore, for the reasons above and of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 51 is rejected under 35 U.S.C. 102(b) as being anticipated by Thornthwaite (US Patent 4,668,618).

Claim 51 is broad encompassing any sequence that contains the human or mouse Ikaros promoter. More specifically, the limitation that the sequence is 'amplifiable' is being interpreted as a possible means of identifying the Ikaros promoter and that at minimum the sequence encompassed by the claims contains the genomic sequence between these two oligonucleotide sequences. The claim does not limit the claimed sequence to a sequence that is amplified. Therefore, any sequence that contains the human or mouse Ikaros gene sequence would anticipate the instant claim.

Thornthwaite describes nuclear isolation media and the methods of use for the isolation of whole nuclear DNA (see summary in abstract). Thornthwaite teaches that at the time of filing the nuclear isolation was known, and that cells from tissue or in culture can be use (see for example column 7, lines 1-17 or claim 14). The media can used for cells from any animal, and Thornthwaite specifically discusses the use with mouse and human peripheral blood samples

(column 5, lines 26-40). Because claim 51 broadly reads on isolated nuclear genomic DNA, the isolated nuclear DNA described by Thornthwaite anticipates the claim.

Conclusion

No claim is allowed. Claims 1, 7-10 and 52-56 are free of the art of record because the art fails to teach or make obvious the regulatory region of the Ikaros gene, however the clams are subject to other rejections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732. After January 12, 2004, the Examiner's telephone number will be (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. After January 12, 2004, Deborah Reynolds telephone number will be (571)272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141. After January 14, 2004, Dianiece Jacobs telephone number will be (571)272-0532.

Joseph T. Woitach